ELECTRICAL STIMULATION ENHANCES CELLULAR / MOLECULAR FUNCTIONS OF OSTEOBLASTS RELEVANT TO NEW BONE FORMATION *IN VITRO*

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I. INTRODUCTION

The static conditions conventionally used in tissue-culture do not represent the biophysical milieu of bone *in vivo* and, thus, leave cells without stimuli which may affect functions pertinent to new bone formation. Bone *in vivo* exists in a dynamic environment subject to various, such as mechanical and electrical, stimuli. There is evidence in the literature that electrical stimulation, specifically, when applied to osteotomies created in animla models, resulted in accelerating healing of the damaged bone (Bassett et al., 1969; Black et al., 1986). These animal studies provided evidence that electrical stimulation promotes bone regeneration and became the impetus to investigate the effects of electrical stimulation at the cellular/molecular level. It is, therefore, our hypothesis that electrical stimulation enhances *in vitro* osteoblast functions that are pertinent to new bone formation. In addition, application of electrical stimulation to tissue engineering endeavors is one possible method to overcome the limitations inherent in new bone formation under static cell culture conditions.

II. RESULTS

The present study used a special custom-designed laboratory setup to expose rat calvarial osteoblasts cultured on current-conducting polylactic acid/carbon nanotube (PLA/CNT) composites to alternating current electrical stimulation (10 μA at 10 Hz) 6 hours daily for up to 21 consecutive days acccording to established techniques (Supronowicz et al., 2001). The effects on cell proliferation were examined by exposing osteoblasts to electrical stimulation for 6 hours daily for 2 consecutive days. Compared to controls (that is osteoblasts cultured without electrical stimulation), the electrical stimulation regime used in the present study resulted in increased (by 46%) cell proliferation. In addition, total calcium produced by osteoblasts exposed to electrical stimulation for 6 hours daily for 21 consecutive days was three-fold greater than that obtained under control conditions. Select genes of bone matrix proteins were differentially expressed under electrical stimulation; for example, and compared to controls, collagen type I gene expression was upregulated at 1, 7, and 21 days when osteoblasts were exposed to

Report Documentation Page

Report Date	Report Type	Dates Covered (from... to)
25 Oct 2001	N/A	-

Title and Subtitle Electrical Stimulation Enhances Cellular/Molecular Functions of Osteoblasts Relevant to New Bone Formation in Vitro	**Contract Number**
	Grant Number
	Program Element Number
Author(s)	**Project Number**
	Task Number
	Work Unit Number
Performing Organization Name(s) and Address(es) Department of Materials Science and Engineering, and Rensselaer Nanotechnology Center Rensselaer Polytechnic Institute Troy, NY 12180-3590	**Performing Organization Report Number**
Sponsoring/Monitoring Agency Name(s) and Address(es) US Army Research, Development & Standardization Group (UK) PSC 802 Box 15 FPO AE 09499-1500	**Sponsor/Monitor's Acronym(s)**
	Sponsor/Monitor's Report Number(s)

Distribution/Availability Statement
Approved for public release, distribution unlimited

Supplementary Notes
Papers from 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, October 25-28, 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom.

Abstract

Subject Terms

Report Classification unclassified	**Classification of this page** unclassified
Classification of Abstract unclassified	**Limitation of Abstract** UU

Number of Pages
2

electrical stimulation for 6 hours daily (Supronowicz et al., 2001).

III. DISCUSSION

The present study applied electrical stimulation to osteoblasts *in vitro* and provided cellular/molecular evidence that alternating current electrical stimulation promotes various important, osteoblast functions, such as cell proliferation, expression of genes for collagenous and non-collagenous proteins, and calcium deposition in the extracellular matrix. These functions are responsible for the chemical composition of the organic and inorganic phases of the bone matrix and are required for new bone formation *in vivo*. Moreover, such functions have major consequences for bone repair, healing, and regeneration and may be responsible for the accelerated bone healing observed in animal models under electrical stimulation. The present *in vitro* research exemplifies the use of biophysical stimuli and alternative strategies for enhancing osteoblast functions which, although extremely promising, remain as yet unexplored for bone regeneration purposes in either clinical or tissue engineering applications.

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